CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

64081

CHEMISTRY REVIEW(S)

1. CHEMIST'S REVIEW NO. 4

2. AADA # 64-081

3. NAME AND ADDRESS OF APPLICANT
Biocraft Laboratories, Inc.
Attention: Jay Snyder
8-10 River Road
Fair Lawn, NJ 07410

4. LEGAL BASIS for ANDA SUBMISSION
21 CFR 442.106(a)

5. SUPPLEMENT(s)
N/A

6. NAME OF DRUG
N/A

7. NONPROPRIETARY NAME
Cefaclor Capsules USP

8. SUPPLEMENT(s) PROVIDE(s) FOR
N/A

9. AMENDMENTS AND OTHER DATES
Date of Application: February 19, 1993
Refuse to File: April 5, 1993
Amendment: April 30, 1993
Chem NA letter - MAJOR: August 16, 1993
Bio NA letter: September 13, 1993
Amendment: May 12, 1994
Chem NA letter - MAJOR: August 31, 1994
Amendment: September 20, 1994
Chem NA letter - MINOR - March 14, 1995
Amendment - March 31, 1995

10. PHARMACOLOGICAL CATEGORY
antibiotic

11. HOW DISPENSED
R

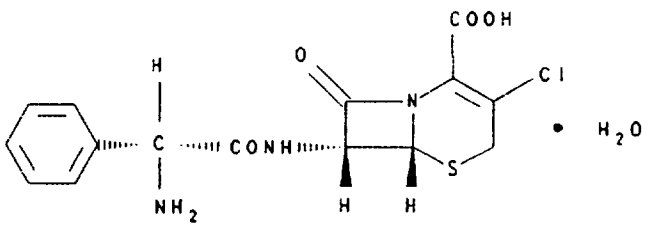
12. RELATED IND/NDA/DMF(s)
AADA 64-072: - Cefaclor Monohydrate drug substance - approved 3/30/95.
DMF's: see DMF checklist

13. DOSAGE FORM
Capsules

14. POTENCY
250 mg & 500 mg capsules

15. CHEMICAL NAME AND STRUCTURE

Cefaclor monohydrate



16. RECORDS AND REPORTS
None

17. COMMENTS
The firm proposes manufacture of Cefaclor Capsules USP with batch sizes of Kg. Exhibit batches of 66 Kg/250 mg and 71.5 Kg/500 mg were manufactured and filled into the market containers - 60 mL/15's, 100 mL/100's, 500 mL/500's 250 mg strength, and 60 mL/15's, 100 mL/100's, 750 mL/500's 500 mg strength. Active drug substance was supplied by approved 3/30/95. The manufacturing process is satisfactory. Accelerated stability were acceptable to support the proposed 24 month expiry.

The following CMC deficiencies communicated to the firm in the NA letter dated 3/14/95 have been responded to:

Deficiency

It is not indicated whether or not you have established a "cut-off" point at which you discontinue the use of recycled materials and begin a new campaign. In addition please specify the maximum holding time, and holding conditions for your recycled material. Also clarify whether capsule contents will be recovered, and, if so, provide a detailed description of the process, master batch records, and specify the conditions for eligibility of a batch for recovery.

Response - ACCEPTABLE

SOP "Procedure for Reclaiming Filled Hard Gelatin Capsules for Addition to a Different Batch" indicates that the capsules are to be held NMT 90 days, and that the expiration dating is based upon the oldest manufactured material in the batch. Only product from the same product and potency will be added, and NMT % of the batch.

The firm had earlier indicated that:
A batch will be comprised of NMT % of recycled material. Tailings will only be added to batches of the same product and potency. The date of initiation of manufacture of the earliest portion of the batch will be used for calculation of product expiry.

In addition to responding to this deficiency, please note and acknowledge the following in your response:

Comment

Please provide any additional stability data which are available to date.

Response - ACCEPTABLE

Additional room temperature stability data through 12 months have been provided. The data are acceptable - it is noted that the total related substances are quite low (< 1%). The 500 mg strength batch , had an initial potency of only 95.75%,

Comment

The referenced bulk antibiotic application has not yet been approved. Until it is approved, this application will remain not approvable.

Response

Acknowledged. N.B. the reference AADA for the bulk drug from was approved 3/30/95.

18. CONCLUSIONS AND RECOMMENDATIONS

RECOMMENDATION: NOT APPROVABLE (cGMP) - MINOR

19. REVIEWER — DATE COMPLETED

Eric P. Duffy, Ph.D.